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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,034	05/25/2001	David Botstein	P2930R1C1	4767

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,034	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action:

Claims 27, 28 and 32-35 are pending and under consideration. The claims have not been amended.

Applicant's arguments regarding the rejections over prior art have been fully considered and are persuasive. The rejections are withdrawn.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 27, 28 and 32-35 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons cited in the previous Office Action mailed 2/9/2004 , at pages 2-4. Applicants traversal filed 5/19/2004 has been fully considered but is not deemed persuasive.

Applicants arguments largely presume that it has been established via the delta Ct data that the gene encoding PRO1800 is *overexpressed* in the tested cell lines. The Examiner does not accept this assertion. As stated in the previous Office action, the data show, at *best*, that the nucleic acid encoding PRO1800, the claimed protein, is present at a level *only twice* that of the control cells. That is *not* considered to be conclusive, or even indicative that the gene is being *overexpressed.* Rather, it establishes that there are twice as many copies of the nucleic acid in the cancerous cell lines that gave a delta Ct value of greater than 1 than in the cancerous cell lines that tested negative, or the non-cancerous cells tested. A two-fold increase in nucleic acid level is more likely to be indicative of aneuploidy than it is of overexpression. The difference is key here. If the result is due to aneuploidy, then the person of ordinary skill in the art would expect that the level of PRO1800 protein, *if present at all*, would not be affected, or would be affected only in a minor fashion. Note that the result does not evidence that PRO1800

protein is being expressed in the cells *at all.* A mere measurement of the amount of nucleic acid present does not inform the person of ordinary skill in the art as to whether that nucleic acid is transcribed and translated in that cell line. The specification contains no information, assertion or data, indicating that the claimed protein was actually expressed in any of the cell lines tested. If the gene were expressed, and if it were expressed at an increased level in the cells, one would reasonably expect a greater than two-fold increase in the amount of PRO1800 nucleic acid present; each gene occurs at two copies per cell, but when it is expressed to produce protein, many more copies are made when transcription to mRNA occurs. Thus, one would reasonably expect a greater than two-fold increase if "normal" cells did not express the protein and "cancerous" cells did. The situation becomes more complex if the "normal" cells express the protein and the cancerous cells overexpress the protein. The specification provides no guidance as to whether PRO1800 protein is present in either normal or cancerous cells, and if so, at what levels. the art does not support the assertion that a two-fold increase in DNA level would be indicative of overexpression of the encoded protein. Rather, the Examiner finds that the Sen reference provides a more parsimonious explanation of the data, that the chromosome that contains the PRO1800 gene is aneuploid in some of the tested cancers.

Applicants assert at page 4 of the response that "the working hypothesis among those skilled in the art is that, if a gene is amplified in cancer, the encoded protein is likely to be expressed at an elevated level." This argument has been fully considered but is not deemed persuasive because applicants have not provided any facts or evidence to support this assertion, other than the Grimaldi declaration, which is discussed below.

The declaration by Dr. Grimaldi has been fully considered but is not deemed persuasive. At paragraph 4, the declarant discusses mutations of Her2/Neu, and chromosomal translocations that are known to be associated with cancer, and states that "If the chromosomal aberration results in the aberrant expression of a mRNA and the corresponding gene product (the polypeptide) as they do in the aforementioned cases, then the gene product is a promising target for cancer therapy, for example, by the therapeutic antibody approach." This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere

invitation to experiment, and not a readily available utility. The PRO1800 gene, unlike Her2/Neu, has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. Similarly, unlike t(5;14), no translocation of PRO1800 is known to occur. All that the specification demonstrates is that the PRO1800 nucleic acid was amplified in 7 of 12 tested human lung tumor squamous cell cancer samples, to a minor degree, of 2-4-fold increase. No mutation or translocation of PRO1800 has been associated with lung tumor squamous cell cancer. It is not known whether PRO1800 is expressed in normal lung tissue or in lung tumor squamous cell cancer, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1800 is amplified in a small number of samples, and invite the artisan to determine the rest of the story. Such is insufficient to meet the requirements of 35 U.S.C. §101 for the claimed protein.

At paragraph 5, Declarant argues that increased mRNA expression is expected to be associated with increased protein production. This argument has been fully considered but is not deemed persuasive because (a) this appears to be Declarant's opinion, and is not supported by fact or evidence (b) there has been no distinction on the record in general or in the specification as filed between total nucleic acid, which includes chromosomal DNA, and mRNA. One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. It remains that there is no information on the record as to whether the claimed protein is expressed *at all* in lung tissue, cancerous or otherwise. It remains that, as evidence by Pennica et al., the issue is simply not predictable, and the specification presents a mere invitation to experiment. This is further borne out by paragraph 6, which proposes further experimentation, should applicants assertions be erroneous.

The Goddard and Ashkenazi declarations are not pertinent, as they are drawn to the significance of the amplification of the nucleic acids encoding PRO1800, and fail to address the issue of the claimed protein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-34 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion:

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number is 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner